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Impaired left ventricular function in lean women with PCOS: insights from speckle tracking echocardiography

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ABSTRACT

Aims: We aimed to conduct a study examining left ventricular function (LVEF) in lean women PCOS patients with speckle tracking echocardiography.

Methods: The study included 60 patients diagnosed with PCOS and 30 healthy controls matched for age and body mass index. Morning fasting blood samples were collected to measure levels of glucose, insulin, high-sensitivity C-reactive protein (hs-CRP), and lipids. Left ventricular function (LVF) was evaluated using two-dimensional speckle tracking echocardiography (2D-STE) and real-time three-dimensional echocardiography (3D-Echo). Global strain was assessed from three standard apical views using 2D-STE.

Results: The hs-CRP levels in lean women with PCOS were significantly higher compared to the control group (2.34±1.07 vs. 1.13±0.54; p=0.01). The peak longitudinal strain values in the 2-chamber, 4-chamber, and long-axis views were lower in lean women with PCOS compared to the control group (15.9±1.2 vs. 19.4±1.2; p=0.01, 17.0±1.1 vs. 19.2±1.4; p=0.01, 16.3±1.3 vs. 19.2±1.5; respectively, p=0.01). According to the multiple regression model, global strain was independently associated with hs-CRP (β=0.31, p=0.04), the ratio of early diastolic mitral inflow velocity (E) to early diastolic annular velocity (E/E' ratio) (β=0.33, p=0.01), and ejection fraction (EF) (β=0.35, p=0.01).

Conclusion: Our findings reveal that lean women with PCOS exhibit significantly higher levels of high-sensitivity C-reactive protein (hs-CRP) compared to healthy controls. Furthermore, the peak longitudinal strain values across multiple cardiac views were notably lower in the PCOS group, suggesting impaired left ventricular function. These results highlight the importance of monitoring cardiovascular health in lean women with PCOS, as they are at an increased risk of developing left ventricular dysfunction despite their lean body mass index.

Keywords: PCOS, high-sensitivity C-reactive protein, echocardiography

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous chronic disease that is common in women of age and causes endocrine and metabolic disorders.[1] PCOS affects 6-10% of women of childbearing age. The prevalence of PCOS in premenopausal women ranges from approximately 6% when older, more restrictive criteria are applied to approximately 20% when more inclusive definitions are applied. It is characterized by menstrual dysfunction, chronic anovulation, polycystic ovaries and hyperandrogenism. It appears that the prevalence of polycystic ovary syndrome varies according to diagnostic criteria. Criteria used to diagnose PCOS; NIH (National Institutes of Health) and Rotterdam criteria.[2] Individuals with PCOS often exhibit high luteinizing hormone (LH), high prolactin, and high androgen concentrations. Additionally, sex hormone binding globulin (SHBG) levels also decrease.[3,4]

The incidence of diseases that cause mortality and morbidity has increased in patients with PCOS. Although the mechanism is not clearly revealed, they are Diabetes Mellitus (DM), Hypertension (HT), Dyslipidemia, and Diastolic Dysfunction.[5,6] Moreover, LVF impairment has been reported to be often associated with obesity and insulin resistance.[7] It is known that increased CVD risk is not only seen in obese women with PCOS. There are studies showing increased CVD risk in lean women with PCOS due to the effect of chronic inflammation.[8,9] In the assessment of LVF, echocardiography is usually used method of choice.

In addition, magnetic resonance imaging (MRI) and scintigraphy techniques are also used.[10] Ejection fraction (EF), tissue Doppler imaging (TDI) and Doppler strain

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are the most commonly used methods in the calculation of LVF.[11] Although, EF is the most commonly used index in LVF assessment, subjectivity and variability depending on the clinician are disadvantages. The most important limitations of the TDI and Doppler strain is limited spatial resolution and angle dependence.[12]

Two-dimensional strain imaging is a newly used method providing both objective and quantitative assessment of left ventricular (LV) functions. In addition, limitations of EF, TDI and Doppler strain are not included in this two-dimensional strain imaging. Thus, two-dimensional strain imaging has been used more frequently in recent years.[13,14]

Many reports evaluated the left ventricular functions in women with PCOS by echocardiographic imaging.[15] Yet, there is no study that investigates the LV functions in lean women with PCOS by two -dimensional speckle tracking echocardiography (2D-STE) method. In the present study we aimed to evaluate subclinical LV functions in lean women with PCOS by 2D-STE method.

METHODS

The study was carried out with the permission of the Adana City Training and Clinical Researches Ethics Committee (Date: 01.05.2024, Decision No: 115). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study population consisted 60 lean women with PCOS who were referred from Department of Obstetrics and Gynecology (mean age, 24.14±5.07) and 30 healthy subjects as controls (mean age, 25.11±7.78 years). The diagnosis of PCOS was defined according to the criteria of 2003 Rotterdam European Society of Human Reproduction and Embryology / American Society for Reproductive Medicine (ESHRE/ASRM).[2] Age, body mass index (BMI) and biochemical blood parameters; and high-sensitivity C-reactive protein (hs-CRP) levels were recorded. The demographic characteristics and clinical data of the patients and the controls are collected.

The control subjects had no history of cardiovascular or other organ system diseases. Their physical examinations, chest X-rays, electrocardiograms, and two-dimensional and Doppler echocardiograms were all normal. Exclusion criteria included diabetes mellitus, renal failure, hypertension, coronary artery disease, chronic obstructive pulmonary disease, thyrotoxicosis, left ventricle ejection fraction below 50%, moderate or severe valvular stenosis and/or regurgitation, a QRS duration over 120 MS, and cardiac arrhythmias. Additionally, patients with poor echocardiographic image quality were excluded. The study was approved by the local ethics committee, and all participants provided written informed consent.

Echocardiographic Measurements

Left ventricular ejection fraction (EF) was calculated using the Simpson method.[16] Pulmonary artery pressure was estimated using the simplified Bernoulli equation, inferior vena cava abundance, and tricuspid regurgitation was estimated using jet velocity.[17]

The patients' left ventricular masses and left ventricular mass index were determined in grams with the widely used formula based on the echocardiographic parameters developed by Devereux and Reichek.[18] Again, body surface area was calculated by taking the height and weight of the patients. Left ventricular mass indexes were calculated by dividing the left ventricular mass by the body surface area. It was calculated with the formula SVK (gr)=0.8 x (1.04 (SVDSç +PDk+IVSk(^{3}-(SVDSç)^3)+0.6.18 Diastolic dysfunctions were categorized according to early and late diastolic mitral inflow (E/A ratio) velocities.[19] Grade 3 diastolic dysfunction was defined by an E/A ratio greater than 2, a Dt less than 140 milliseconds, and an E/E' ratio exceeding 10.[20] All imaging assessments were conducted by two cardiologists who were blinded to the participants' clinical information

Two-Dimensional Echocardiography

Evaluation of two-dimensional echocardiography images was performed using left ventricular (LV) apical four-chamber (4C), long-axis (LAX), and two-chamber (2C) views. All images were captured during a breath hold and stored in cine-loop format from three consecutive beats.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) program for Windows Version 27.0 (SPSS, Inc., Chicago, IL, USA) was utilized for the statistical analysis. Results were reported as the mean±SD, and categorical variables were presented as percentages. The chi-squared test was applied for the statistical analysis of categorical variables. The Mann–Whitney U-test was used for differences between lean women with PCOS and the healthy group. Correlation analyses were used. Additionally, Bland–Altman analysis was used to assess inter- and intra-observer variability in left ventricular deformation parameters. A p-value of <0.05 was considered statistically significant for all statistical analyses.

RESULTS

The demographic characteristics, clinical features, laboratory results, and medications of the study groups are presented in Table 1. The PCOS patients and healthy subjects were similar in age, body mass index (BMI), fasting glucose, fasting insulin, HOMA-IR, cholesterol levels, smoking habits, and alcohol consumption. However, the mean±SD hs-CRP values were significantly higher in lean patients with PCOS compared to the healthy subjects (2.34±1.07 mg/L vs. 1.13±0.54 mg/L; p<0.01).

The baseline echocardiographic values are detailed in Table 2. There were no significant differences in ejection fraction (EF), left ventricular mass (LVM) index, left ventricular (LV) diameter, or left atrium diameter between patients with PCOS and healthy controls. However, diastolic dysfunction was observed in three (10.0%) of the control subjects and in 18 (30.0%) of the PCOS patients, with all 18 PCOS patients displaying Grade 1 diastolic dysfunction and none showing Grade 2 or 3 diastolic dysfunction. Lean women with PCOS had elevated values for isovolumetric relaxation time (IVRT), deceleration time (Dt), peak A velocity, and E/E' ratio. In contrast, the control group exhibited a higher E/A ratio

Table 1. The demographic and clinical characteristics, as well as laboratory findings, in lean women with PCOS and control subjects

	PCOS (n=60)	Control group(n=30)	p
Age, years, mean±SD	24.14±5.07	25.11±7.78	NS
Body mass index, kg/m2, mean±SD	21.4±2.1	22.5±2.3	NS
Smoking, n(%)	13 (18.1)	4 (12.9)	NS
Alchol, n(%)	4 (5.5)	3 (9.6)	NS
Total cholesterol mg/dl, mean±SD	158±21	164±32	NS
LDL cholesterol, mg/dl, mean±SD	120±21	116±19	NS
HDL cholesterol, mg/dl, mean±SD	35±8	33±7	NS
Plasma triglyceride, mg/dl, mean±SD	163±38	148±32	NS
hs-CRP, mg/L, mean±SD	2.34±1.07	1.13±0.54	<0.01
Fastıng glucose, mg/dl	84.4±1.1	87.2±9.7	NS
Fasting insulin, Miu/Liter	10.4±3.4	9.8±2.6	NS
HOMA-IR	2.16±0.7	2.11±0.4	NS

HDL: High-density lipoprotein, hs-CRP: High-sensitivity C-reactive protein, HOMA-IR: Homeostatic model assessment-insulin resistance, LDL: Low-density lipoprotein NS: Non-significant (p>0.05)

Table 2. Echocardiographic findings in lean women with PCOS and control subjects

	PCOS group (n= 60) Mean±SD	Control group (n=30) Mean±SD	p
LV end-diastolic dimension, cm	2.68±0.39	2.65±0.33	NS
LV end-systolic dimension, cm	4.64±0.39	4.58±0.35	NS
IVSD, cm	0.99±0.09	0.99±0.065	NS
LVPWD, mm	0.99±0.09	0.99±0.06	NS
LA, mm	32.3±2.8	31.4±3.8	NS
Ejection fraction, %	64.14±2.43	64.67±2.53	NS
LV mass index, g	146.2±28	145.9±30	NS
E, cm/s	75.9±10.9	77.2±11.4	NS
A, cm/s	76.2±10.8	70.1±12.2	<0.01
E/A ratio	1.06±0.28	1.17±0.18	<0.01
Deceleration time, ms	216±32	178±29	<0.01
IVRT, ms	98±13	80±8	<0.01
E/E' ratio	8.3±1.8	7.4±1.3	<0.01

A: Late diastolic mitral inflow, E: early diastolic mitral inflow velocity, E/E0: Ratio of early diastolic mitral inflow velocity to early diastolic annular velocity, IVRT: Isovolumetric relaxation time, IVSD: Interventricular septum diameter, LA: Left atrium, LV: Left ventriculi, LVPWD: Left ventricular posterior wall diameter. NS: Non-significant (p>0.05)

When comparing data between the control and PCOS groups, it was found that left ventricular global strain (LV-GS), four-chamber longitudinal strain (4C-LS), long-axis longitudinal strain (LAX-LS), and two-chamber longitudinal strain (2C-LS) values were significantly lower in the lean PCOS group. Additionally, all strain rate (SR) values were significantly reduced in patients with PCOS compared to healthy subjects (Table 3).

A multiple regression model was established with global strain (GS) as the dependent variable, along with hs-CRP, EF, E/A ratio, and E/E' ratio as independent variables. The analysis showed that GS was independently associated with hs-CRP (β=0.31, P=0.04), E/E' ratio (β=0.33, p=0.01), and EF (β=0.35, p=0.01). Similarly, in a multiple regression model for global strain rate (GSR) with hs-CRP, E/A ratio, E/E' ratio, and EF, GSR was independently associated with EF (β=0.32, p<0.01) and E/E' (β=0.31, p<0.01) (Table 4).

Table 3. Left ventricular two-dimensional strain and strain rate measurements in lean women with PCOS and control subjects

	PCOS group (n= 60) Mean±SD	Control group(n=30) Mean ± SD	p
2C-SR, per s	1.31±0.32	1.52±0.34	0.02
LAX-SR, per s	1.26±0.27	1.46±0.32	<0.01
4C-SR, per s	1.29±0.35	1.65±0.40	<0.01
GS, %	16.2±1.3	19.1±1.8	<0.01
GSR, per s	1.42±0.24	1.54±0.32	<0.01
2C-LS, %	15.9±1.2	19.4±1.2	<0.01
LAX-LS, %	16.3±1.3	19.2±1.5	<0.01
4C-LS, %	17.0±1.1	19.2±1.4	<0.01

2C: Two-chamber, 4C: Four-chamber, GS: Global strain, GSR: Global strain rate, LAX: Parasternal long axis, LS: Longitudinal strain; SR: Strain rate.

Table 4. Correlations between echocardiographic parameters and global strain (GS) and global strain rate (GSR) values

	Global strain				Global strain rate			
	p	p-value	B	p-value	p	p-value	B	p-value
Hs-CRP	0.32	0.01	0.31	0.04	0.33	0.01	0.28	0.06
E/A ratio	-0.32	0.03	-0.25	0.07	-0.31	0.02	-0.23	0.06
E/E' ratio	-0.34	<0.01	-0.33	0.01	-0.30	<0.01	-0.32	<0.01
EF	0.41	0.01	0.35	0.01	0.37	<0.01	0.31	<0.01

EF: Ejection fraction, E/A: Ratio of early to late diastolic mitral inflow velocities, E/E': Ratio of early diastolic mitral inflow velocity to early diastolic annular velocity.

DISCUSSION

In this study, we investigated left ventricular function using two-dimensional strain imaging in lean PCOS patients. Our findings revealed that lean PCOS women have reduced LV systolic longitudinal function compared to the healthy group.

PCOS patients generally characterized by obesity, hypertension, insulin resistance, and dyslipidemia. Frequent occurrence of cardiovascular risk factors suggests that this is associated with increased risk of cardiovascular system (CVS) in PCOS patients.[6,15,21]

Studies on CVS morbidity and mortality in PCOS are not yet sufficient. In United Kingdom, women with PCOS followed for 30 years, and increased mortality was observed in the CVS.[22] In contrast, in patients with menstrual irregularities in the Nurses' Health study had an increased fatal or non-fatal CVS risk.[23] Additionally, in a study angiography results of postmenopausal women who are at risk of ischemia revealed that women with PCOS have increased CVD incidence.[24]

High-sensitivity CRP is a sensitive marker of inflammation. It is used to predict and diagnose low-grade inflammatory conditions. Its increase seems to be related to the extent of tissue injury and severity of inflammation. In patients with PCOS, levels of hs-CRP are expected to be high as a result of chronic inflammation. Also, CRP, predictor of CVD, was found to be increased in patients with PCOS.[25-27] Consistent with these findings, in our study CRP levels were found to be higher in PCOS patients. After adjustment for BMI in PCOS patients, some studies reported no difference in CVD mortality and some reported increased CVD mortality.[28,29] Also, in the present study, we determined a decrease in left ventricular functions in PCOS patients with BMI.

Numerous echocardiographic studies were attempted to investigate the presence of subclinical CVD in patients with PCOS. Diastolic LV dysfunction is known to be related to CVD risk. It is found that PCOS patients had a decrease in left ventricular diastolic function.[30] Sub clinic myocardial dysfunction may occur in PCOS patients. 2D-STE can be useful to show subclinical myocardial dysfunction.[31] It has been scientifically demonstrated that strain imaging, which has been widely used in recent years, more clearly demonstrates subclinical left ventricular dysfunction that conventional echocardiography cannot detect.[32] Erdogan et al.[33] used 2D-STE method and reported an impairment in left ventricular diastolic function and a reduction in global strain values. In their study, the average BMI of patients is 29.4+8.5. Obesity itself increases the risk of CVD. Although our study population was consisted of lean women with PCOS, GLS values were found to be increased. Moreover, a correlation was found between hs-CRP, which indicates subclinical inflammation, and GLS.

Left ventricular ejection fraction (LVEF) is usually measured to evaluate for LV systolic function.[31,34] In the current study, we found no differences in LV diameter, EF, left atrium diameter and LVM index between subjects with and without PCOS. However, in patients with PCOS, diastolic dysfunctions were detected more frequently. Additionally, LV strain and all SR values were found to be significantly lower in patients with PCOS than in control subjects.

As the experience of operator, image quality and LV geometry's assumption, C-echo gives limited data to us. The mechanism of 2D-STE is founded to following of characteristic speckle patterns occurred by initiative of ultrasonographic beams from myocardium. Speckle tracking is superior to evaluate for longitudinal function of left ventricle to basal segments. Longitudinal contraction is used to evaluate the subendocardial function in subclinical cardiovascular diseases like PCOS. While the LVEF of lean women with PCOS were normal using C-echo, LVEF values also in the same group were impaired using 2D-STE compatible with our knowledge mentioned above.

Limitations

The major limitation of our study is relatively small number of study population. Because of case control study, we could not have opportunity to evaluate echo results of drugs administrated in PCOS. Therefore, we do not know what will be the outcome of subclinical echo results in the future. Also, technical limitations of speckle echo can be seen our study.

CONCLUSION

This study highlights significant cardiac involvement in lean women with PCOS, demonstrating that these patients exhibit impaired left ventricular function as evidenced by lower peak longitudinal strain values in the 2-chamber, 4-chamber, and long-axis views. The findings also indicate that global strain is independently associated with elevated hs-CRP levels, increased E/E' ratio, and decreased ejection fraction (EF). These results suggest that even lean women with PCOS, who might be considered at lower risk due to their body mass index, are nonetheless at a heightened risk for cardiovascular complications. Early detection and monitoring of cardiac function using advanced imaging techniques like speckle tracking echocardiography can be crucial for managing and mitigating the cardiovascular risks associated with PCOS.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Adana City Training and Clinical Researches Ethics Committee (Date: 01.05.2024, Decision No: 115)

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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